DEC 2003

This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150. See reverse for additional information.

Interagency Report Control No. 0100180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 10-F-0002 CUSTOMER NO. 439

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)

WALTER REED ARMY INSTITUTE OF RESEARCH
DIV. OF VETERINARY MEDICINE
BUILDING 511
WASHINGTON, DC 20307
(301) 319-9897

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS(sites)

See Attached Listing	Experimental Therapeutics, Neuroscience, Biochemistry
Division of Veterinary Medicine .	
Military Casualty Research, Infectious Diseases, Retrovirology	Communicable Diseases & Immunology, Combat Casualty Care

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY Attach additional *sheets if necessary* or use *APHIS FORM 7023A*)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An *explanation of the procedures producing pain or distress in these animals* and the reasons *such drugs were* not used must be attached to *this* report)	F. TOTAL NO. OF ANIMALS (Cols. C + D+E)
4. Dogs	0	0	31	0	31
5. Cats	0	0	0	0	0
6. Guinea Pigs	0	10	53	304	367
7. Hamsters	0	27	134	0	161
8. Rabbits	0	122	51	1	174
9. Non-Human Primates	92	327	228	8	563
10. Sheep	0	0	0	0	0
11. Pigs	1	66	212	46	324
12 Other Farm Animals					
13. OtherAnimals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all the exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)

I certify that the above IS true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED
		DEC 16 2003

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete PART 1 - HEADQUARTERS

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 10-F-0002

2. Number 1 of animals used in this study.

3. Species (common name) Rabbit of animals used in the study.

4. Explain the procedure producing pain and/or distress.

Distress due to Busulfan/Ethyl palmitate, the cytotoxic regimen, or due to antibodies used to induce thrombocytopenia in rabbits, may weaken the animal and cause potential symptoms, such as: significant bleeding due to thrombocytopenia (hematoma); nonspecific drug-related adverse events—persistent anorexia, significant injection site reactions, significant decreased ambulation or listlessness; restlessness, repetitive locomotion, and abnormal vocalization.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Any rabbits showing any combination of these signs will be euthanized with euthanasia solution. All other procedure will occur under general anesthesia in these non-survival experiments, so no pain is anticipated. The potential painful procedures, i.e. the cannulation and laparotomy procedures, described in this protocol are essential for creating the conditions necessary to study the stability and efficacy of Multi-function Blood Substitution in vivo. However, every effort will be made to ensure maximum comfort of the animals under anesthesia. There will be a conscious effort by the P.I. and his staff to provide additional consideration for comfort and well being of the animals as is consistent with the scientific integrity of the study. The attending veterinarian was consulted regarding appropriate and humane use of anesthesia to alleviate the pain associated with the surgical procedures in this protocol. Animals that appear distressed or moribund will be euthanized according to section V.D.7 of this protocol.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency _____ CFR _____

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1. Registration Number: 10-F-0002

2. Number 272 of animals used in this study.

3. Species (common name) Guinea Pig of animals used in the study.

4. Explain the procedure producing pain and/or distress.

Shigella vaccine candidates were evaluated by placing Shigella in the conjuctivae of guinea pigs' eyes, and then the severity of inflammation was scored.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

The study of immune response to and protective effieacy of vaccine candidates directed against Shigella requires an accurate evaluation of the immune response raised by the administration of these vaccines. The use of analgesics, particularly opiates or narcotics, result in immunosuppression, which would invalidate the results of experiments testing immune responses as well as increasing the severity of the possible eye infection. Use of analgesics that are anti-inflammatory (e.g. aspirin) would also invalidate the model since we are studying a model for inflammation of epithelial cells by bacterial invasion.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

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1. Registration Number: 10-F-0002

2. Number 8 of animals used in this study.

3. Species (common name) Rhesus of animals used in the study.

4. Explain the procedure producing pain and/or distress.

Determine if virulent Brucella melitensis strain 16M can establish acute brucellosis in a non-human primate model that is indistinguishable from the aerosol route of infection when given by either conjunctival or nasal routes of infection at identical doses. We expect the organisms to be internalized within the mucosa and subsequently become localized within resident phagocytic cells residing in the mucosa-associated lymphoid tissues. These cells or an unidentified cell population will transport the organisms via the reticuloendothelial (RE) system to target organs. It is expected that the organisms will replicate inside endosomes/phagolysosomes of phagocytic cells and establish acute brucellosis identical to that seen in aerosol studies.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

If illness occurs following the administration of virulent Brucella in animals it will cause some distress. It is unclear whether such distress can be relieved with known treatments that may affect experimental results. Previous experience with rhesus monkeys given high respiratory doses of virulent Brucella indicates when clinical signs (recumbency and weakness, progressive state of depression, inappropriate responses to external stimuli, forced abdominal respirations or dyspnea) have been manifested, illness is evident, however; the animals may recover spontaneously. Narcotic analgesics cause histamine release (Soma 1983). There is evidence for histamine involvement in the simian Brucella responses (Scheuber et al., 1985). Neuroleptanalgesics can cause respiratory depression, bradycardia, and poor muscle relaxation (Swainsbury et al., 1989). Butorphanol tartrate has respiratory depressant activity and causes significant decreases in heart rate, blood pressure, and cardiac output (Lumb and Jones, 1984). Because of the potential for analgesics to contribute to or exacerbate the symptoms of shock, it is unwise to use them in this protocol.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency _____ CFR _____

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1. Registration Number: 10-F-0002

2. Number 32 of animals used in this study.

3. Species (common name) Guinea Pig of animals used in the study.

4. Explain the procedure producing pain and/or distress.

The guinea pigs will be exposed to subacute or to chronic low-dose Soman, Sarin, or VX. Neurological observations will be performed before, during, and following dosing.

Some nerve agent-exposed guinea pigs will be prepared using biotelemetry techniques for the collection and analysis of EEG, EKG, body temperature, and locomotor acitivity data. Guinea pigs will be anesthetized to achieve deep surgical anesthesia using a solution containing a mixture of Ketamine and Xylazine. Having achieved deep surgical anesthesia, either the surgical procedures or euthanasia will be conducted.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Nerve agent exposed Guinea pigs may experience seizures. The pre- and post-seizure periods may be accomplished by distress. The relief of the pre-seizure period of distress is difficult to predict and pharmacological treatment is contraindicated if we are to determine the primary effects of nerve agent exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency _____ CFR _____

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1. Registration Number: 10-F-0002

2. Number 46 of animals used in this study.

3. Species (common name) Swine of animals used in the study.

4. Explain the procedure producing pain and/or distress.

Piglet model for both emetic and lethal response to Staph endotoxins (SE). Piglets are dosed orally with SE. A determination is made of the value of various potential drugs for prophylaxis against emesis (vomiting) and lethal shock. In addition, an evaluation of how late the drugs can be administered after SE-challenge and still retain desired efficacy of response is determined.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

The lethal shock that is induced by the lethal SE-challenge with the LD50 test in the positive control animals will necessarily cause pain to these animals. Positive controls are required to validate results. Analgesics would impact the physiological parameters, exacerbating the lethal shock or emesis induced by the SE and compromising analysis of collected data. If the experimental drugs proved their utility, the animals should experience relief, but should they not experience relief then that indicates failure of the drug and is necessary for that reason. In all circumstances, the animals will be under constant veterinary care and will not be subject to any unnecessary pain.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency _____ CFR _____